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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,391	10/28/2003	Jeffrey Isner	47624-CIP (71417)	6371

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/696,391	ISNER ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-52,54-65 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-52,54-65 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 1/12/06 was entered for the sake of a compact prosecution, even though amended claim 49 still does not comply with the requirement of 37 CFR 1.121 (c) because the existing period at the end of the claim is underlined. Please note that only added subject matter is underlined.

Amended claims 49-52, 54-65 and 68 are pending in the present application, and they are examined on the merits herein.

Response to Amendment

The rejection under 35 U.S.C. 102(b) as being anticipated by Isner (WO 97/14307) was withdrawn in light of Applicant's amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-52, 54-65 and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This is a new ground of rejection necessitated by Applicant's amendment.***

Claim 49 contains the trademark/trade name "NOGA system". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35

U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a system for electromechanical mapping and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

Claims 49-52, 54-65 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isner (WO 97/14307; Cited previously) in view of Hammond et al. (US Patent 5,880,090; IDS) and Dillmann et al. (US 6,605,274; Cited previously). ***This is a new ground of rejection necessitated by Applicant's amendment.***

The instant claims are directed to a method for inducing new blood vessel growth in myocardial tissue of a mammal in need of such a treatment comprising: a) administering an effective amount of a solution comprising a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the muyocardial tissue; and b) administering to the mammal an effective amount of at least one angiogenic factor or an effective fragment thereof, thereby inducing the new blood vessel growth in the myocardial tissue of the mammal, and increasing the frequency of endothelial progenitor cells in the mammal; and c) monitoring a cardiac function by

echocardiography, ventricular end-diastolic dimension, end-sytolic dimension, fractional shortening, wall motion score index, electromechanical mapping with a NOGA system, cardiac angiography or LV systolic pressure. With respect to claims 50-51 and 57, the examiner interprets the term "the angiogenic factor protein" to be the angiogenic protein recited in step (a) of claim 49, because that is the only step where any angiogenic protein is recited.

Isner teaches a method for enhancing blood vessel formation or angiogenesis in an ischemic tissue in a mammal having cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy and **myocardial ischemia** (page 4, lines 5-23). The method comprises the step of injecting said tissue with an effective amount of a nucleic acid capable of expressing an angiogenic protein by any injection means, and the nucleic acid may be carried by vehicles such as cationic liposomes, adenoviral vectors and that **nucleic acid encoding different angiogenic proteins may be used separately or simultaneously** (page 4, line 25 continues to line 8 of page 5). **Angiogenic protein includes aFGF, bFGF, VEGF (including VEGF165, see page 15, line 19), EGF, PDGF, PD-ECGF, HGF, colony stimulating factor (CSF), macrophage-CSF (M-CSF), granulocyte/macrophage CSF (GM-CSF) and nitric oxide synthase or muteins or portions thereof** (page 5, lines 10-22). Isner also teaches that the nucleic acid encoding an angiogenic protein is inserted into a cassette where it is operably linked to a promoter that is capable of driving expression of the protein in cells of the desired target tissue (page 9, line 28 continues to line 20 of page 10). **Isner further teaches that an angiogenic factor can**

be combined with other genes or their encoded gene products to enhance the activity of targeted cells, while simultaneously inducing angiogenesis, including, for example, nitric oxide synthase, L-arginine, fibronectin, urokinase, plasminogen activator and heparin (page 11, lines 15-19). Isner also discloses that catheters have been used for gene delivered in the art (page 1, line 23 continues to line 30 of page 2).

Isner does not teach specifically the administration of an effective amount of a stem cell factor (SCF), a colony stimulating factor (CSF) or an effective fragment thereof into the mammal to induce new blood vessel growth and to increase the frequency of endothelial progenitor cells, even though Isner teaches that nucleic acids encoding different angiogenic proteins such as aFGF, bFGF, VEGF (including VEGF165, see page 15, line 19), EGF, PDGF, PD-ECGF, HGF, colony stimulating factor (CSF), macrophage-CSF (M-CSF), granulocyte/macrophage CSF (GM-CSF) and nitric oxide synthase or muteins or portions thereof may be used separately or simultaneously; and that an angiogenic factor can be combined with other genes or their encoded gene products to enhance the activity of targeted cells. Isner also does not teach specifically to monitor a cardiac function by one of the recited approaches, even though Isner discloses monitoring collateral artery development in the medial thigh by angiography (page 21, lines10-25) or measuring calf blood pressure for physiologic assessment (page 22, liens 12-27).

At the filing date of the present application (10/28/03) Hammond et al already taught that cytokines such as stem cell factor (SCF), granulocyte-macrophage colony-

stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF) are capable of mobilizing bone-marrow derived endothelial cell progenitors or non-adherent CD34+ cells in the blood for increasing endothelialization in a treated patient (see at least Summary of the invention). Hammond et al further note that CD34+ circulating cells in the blood can participate in the repair of ischemic tissue (col. 3, lines 28-37).

Dillmann et al already taught that clinical signs of improvement in cardiac performance and accommodation of stresses associated with congestive heart failure (CHF) are well known to those of ordinary skill in the cardiological art and may be determined, for example, by monitoring blood flow, cardiac pumping volume and ventricular pressure by for example, angiography and echocardiography, calcium transport rates, tolerance studies (col. 14, lines 14-26), as well as measurements of left ventricular end-diastole dimension (LVEDD), LV end-systolic dimension (LVESD), and fractional shortening (col. 25, line 37 continues to line 5 of col. 26).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the method of Isner by further administering specifically to the treated mammal an effective amount of at least one of SCF or CSF or an effective fragment thereof to induce new blood vessel growth and to increase the frequency of endothelial progenitor cells in the treated mammal in light of the teachings of Hammond et al. Additionally, it would also have been obvious for an ordinary skilled artisan to monitor the cardiac function in the mammal treated for myocardial ischemia using any of the means recited in claim 49 in light of the teachings of Dillmann et al.

An ordinary skilled artisan would have been motivated to carry out the above modifications because Hammond et al. already demonstrated that cytokines such as stem cell factor (SCF), granulocyte-macrophage colony-stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF) are capable of mobilizing bone-marrow derived endothelial cell progenitors or non-adherent CD34+ cells in the blood for increasing endothelialization in a treated patient; and this mobilization of endothelial cell progenitors would further enhancing blood vessel formation or angiogenesis in an ischemic tissue in a mammal having a myocardial ischemia, and thus further optimizing the desired therapeutic outcome. Additionally, any of the means to monitor cardiac function taught by Dillmann et al is well-known and conventionally used by those of ordinary skill in the cardiological art to monitor clinical signs of improvement in cardiac performance, particularly for the treatment of ischemic cardiomyopathy and/or myocardial ischemia in this instance. It is further noted that the monitoring means is not the patentable subject matter for the claimed methods because Applicants specifically state "cardiac function is monitored in the mammal by one or more combination of standard approaches to evaluate therapeutic outcome" (page 12, lines 24-25). The modified method resulting from the combined teachings of Isner, Hammond et al., and Dillman et al. is indistinguishable from the presently claimed method.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Isner, Hammond et al., and Dillman et al., coupled with a high level of skill for an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

Claims 49-52, 54-65 and 68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 49-61 and 63-66 of copending Application No. 10/714,574 in view of Dillmann et al. (US 6,605,274; Cited previously). ***This is a new ground rejection necessitated by Applicant's amendment.***

The instant claims are directed to a method for inducing new blood vessel growth in myocardial tissue of a mammal in need of such a treatment comprising: a) administering an effective amount of a solution comprising a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the muyocardial tissue; and b) administering to the mammal an effective amount of at least one angiogenic factor or an effective fragment thereof, thereby inducing the new blood vessel growth in the myocardial tissue of the mammal, and increasing the frequency of endothelial progenitor cells in the mammal; and c) monitoring a cardiac function by echocardiography, ventricular end-diastolic dimension, end-sytolic dimension, fractional shortening, wall motion score index, electromechanical mapping with a NOGA system, cardiac angiography or LV systolic pressure.

Claims 49-61 and 63-66 of copending Application No. 10/714,574 are drawn to a method for treating ischemic myocardial tissue of a mammal in need of such a

treatment comprising: a) identifying a mammal which has, is suspected of having, or will have the ischemic tissue; b) injecting an effective amount of a solution comprising a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the muyocardial tissue; and c) administering to the mammal an effective amount of at least one of: stem cell factor, colony stimulating factor or an effective fragment thereof, thereby treating ischemic myocardial tissue of the mammal.

The claims of the present application differ from the claims of the copending Application No. 10/714,574 in reciting the additional step of monitoring a cardiac function by any one of the approaches recited in the Markush group of claim 49.

At the filing date of the present application, Dillmann et al already taught that clinical signs of improvement in cardiac performance and accommodation of stresses associated with congestive heart failure (CHF) are well known to those of ordinary skill in the cardiological art and may be determined, for example, by monitoring blood flow, cardiac pumping volume and ventricular pressure by for example, angiography and echocardiography, calcium transport rates, tolerance studies (col. 14, lines 14-26), as well as measurements of left ventricular end-diastole dimension (LVEDD), LV end-systolic dimension (LVESD), and fractional shortening (col. 25, line 37 continues to line 5 of col. 26).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time the invention was made to modify the method of the copending Application No. 10/714,574 by further monitor the cardiac function in the mammal treated for myocardial

ischemia using any of the means recited in claim 67 in light of the teachings of Dillmann et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because any of the means to monitor cardiac function taught by Dillmann et al is well-known and conventionally used by those of ordinary skill in the cardiological art to monitor clinical signs of improvement in cardiac performance, particularly for the treatment of ischemic cardiomyopathy and/or myocardial ischemia in this instance.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of the copending Application No. 10/714,574 and Dillmann et al., coupled with a high level of skill of an ordinary artisan in the relevant art.

Therefore, the claimed invention was *prima facie* obvious in the absence of evident to the contrary.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusions

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, Celine Qian, Ph.D., may be reached at (571) 272-0777, or SPE, Dave Nguyen, at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

CELINE QIAN, PH.D.
PRIMARY EXAMINER